

EPIDEMIC ENCEPHALITIS, AND THE BENEFICIAL EFFECTS
OF COLLOSOL MANGANESE IN THE ACUTE STAGE.

by

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OF COLLOSOL MANGANESE IN THE ACUTE STAGE.

Since the first recognition of Epidemic Encephalitis or Encephalitis Lethargica as a specific infective disease numerous cases have been observed and described in various parts of the British Isles.

The earliest sufferers in Britain appeared in localities quite distant from one another and the type of case was generally of what is known as a Lethargic nature, giving rise to the name of Encephalitis Lethargica. Lethargy and drowsiness, followed by coma, were the prominent symptoms. The mortality was high reaching, as far as can be ascertained, in the neighbourhood of fifty per cent.

From the year 1918 onwards cases became much more common and in 1924 outbreaks were so pronounced as to assume almost epidemic form in some parts of the country, particularly and naturally where the population was densest. During this same period there seemed to be a gradual change in the general symptoms of the disease; the type seemed somewhat milder in character, and in contrast to the general Lethargy of earlier cases there were distinct restlessness, irritability, marked muscular movements and insomnia in a large proportion of those affected. Coincidentally with/

with this there was a gradual but ultimately a pronounced fall in the mortality rate as is illustrated by the following table:-

<u>Year.</u>	<u>Cases Notified.</u>	<u>Deaths.</u>
1919	541	264
1920	890	471
1921	1470	724
1922	454	337
1923	1025	530
1924	5039	1419

These figures from the Ministry of Health Report show in 1924 the fall of the mortality percentage to below thirty. This figure is probably much higher than the death rate from encephalitis now, but in addition to the general amelioration of the condition one has to consider the benefits derived from more efficient treatment.

The reason for the obvious change in the general symptomatology would seem to be a direct result of the decrease in virulence of the attack as many of the more serious cases, which in the earlier stages were irritative in nature, became lethargic with advancement of the infective process. The majority of cases latterly would seem then to have escaped this more serious prolongation by means of a relatively stronger antagonism/

antagonism within the body. A change in the virulence of the virus or even an alteration in climatic conditions or medium of growth would also be influential factors in deciding the result of infection of the human being.

MODE OF INFECTION.

It is generally accepted that the infective agent is transported by "Carriers" who excrete the virus in their nasal secretions and saliva.

The virus has been produced from the nasal discharges of affected persons and transferred to the cornea of a rabbit, producing a pustular appearance there, and followed by a general degenerative change in the animal resulting in death.

The infective material has been shewn to pass through a filter and can also be preserved potent in glycerine for some considerable time.

As a result of the above means of spread or transportation of the virus, cases of the disease occur much as do those of anterior poliomyelitis, - one here and one there without any very obvious source of contamination.

ALLIED/

ALLIED CONDITIONS.

Outbreaks of Epidemic Hiccough and also mildly febrile states simulating influenzal attacks have been described as having a close connection with the graver disease as they have occurred in families when one member has developed a "true" Encephalitis.

It is reasonable to believe that the disease is sometimes so mild in its onset as to produce only a slight febrile state without the development of sequelae. Again there have been many cases of pronounced Encephalitis which have shewn hiccough as one of their most aggravating and alarming symptoms.

It is generally held that Poliomyelitis, which tends to be sudden in its onset and maximal, has no connection with Epidemic Encephalitis. The regions affected in the former disease are usually innervated from the spinal-cord and the distribution is more often unilateral. There is frequently permanent damage in the area first affected.

POST-MORTEM EXAMINATION.

Pathologists have described four different changes which may take place within the brain and spinal cord, e.g.:-

(a)/

- (a) Infiltration of the walls of small vessels, especially veins, consisting of lymphocytes and plasma cells in the adventitia, and dispersed in several layers.
- (b) Foci of Interstitial cells apart from the area of hyperaemia.
- (c) Various chromatic and degenerative changes within the nerve cells.
- (d) Numerous haemorrhages surrounding the smaller vessels without apparent rupture of their walls.

These changes are mainly in the Basal Ganglia and around the Brain Stem and the variations of symptomatology are then produced by the amount of involvement, the method of involvement, and the nerve centres and tracts complicated.

We have, therefore, a means of localising the morbid process when nerve palsies occur as a result of localised haemorrhagic areas. But there is not the same precision in localisation when only inflammatory or pressure effects exist. The interassociations of the Basal Ganglia are so complicated that any slight pressure from inflammatory exudation around the nerve fibres may elucidate externally numerous symptoms as a result of variations in muscular tone.

Pressure within the brain may be intracellular, extracellular/

extracellular, or it may be directed upon the nerve fibres with the result that there may be numerous variations of motor, sensory or trophic nerve disturbances as well as psychic changes.

These psychic symptoms usually appear as an inhibition of the function of some higher centre or by the removal of the natural control over these areas. Amongst these are changes in character, which are so minute as to pass unnoticed or so gross as to be dangerous.

RATE OF ONSET.

In addition to the intracranial disruption one has to consider the celerity with which those pathological changes occur. Thus a case which progresses slowly shows a sequence of symptoms related to each other and recognisable as an advancement of the process. But in a case of sudden onset the parts are affected so rapidly with the spread of infection that only the resultant salient symptoms are noticable.

Thus one is able to classify all cases roughly in one of two large groups:-

- (a) Apoplectic Type:- where the main symptoms are manifest almost immediately.
- (b) Progressive Type when various symptoms appear during days or weeks ultimately reaching the maximal in Delirium or Coma.

In this latter group the progress of symptoms and the general extent of the disease may be manifestly modified by various factors. The immediate health and natural resisting powers of the patient may terminate the disease at any stage with sudden loss of symptoms and subsequent recovery. Nervous exhaustion and conditions exerting a severe strain upon metabolism (e.g. Pregnancy) may produce a more rapid and fatal termination.

So as a result of the part played by all factors antagonistic to disease we have a grouping of cases to include roughly the various results of infection:-

TYPE I.

Influenzal Type which is more or less taken for granted as the symptoms are so mild as to be undistinguishable from those of any slight febrile condition.

TYPE II.

Acute Type with absolute or almost absolute cure.

TYPE III.

Acute Type with apparent cure, to relapse at a later date.

TYPE IV.

Acute Type passing directly into a chronic form.

Of the above the Influenzal Type need not be further discussed.

The onset of the latter three groups, or of the Acute phase, calls for great consideration as it is here that the Physician must form a diagnosis and be able to furnish anxious relatives with a prognosis. If he can diagnose Acute Encephalitis he can give a hopeful prognosis especially in contrast with other conditions which are liable to be a source of confusion. Amongst these are meningitis of meningococcal and pyogenic origin, T.B. Meningitis, Tumour of Brain, Botulism and Cerebral Haemorrhage.

Generally however a few days have passed before one considers the possibility of any condition other than "Cold", but sooner or later one discovers that headache becomes intense or that there is general nervous disturbance with an increase of Knee Jerks, while the temperature remains the same or even tends to drop. Of the outstanding symptoms to appear at this stage the commonest are;- Double vision, nerve paralysis, myoclonic movements, lethargy, change in character, mood, or habits, intense headache, and sleeplessness.

Unfortunately it is impossible to give any definite sequence of symptoms, but in those cases which I shall describe later it will be seen that antagonistic symptoms, such as are included in the above/

above list, may arise at different stages in the same case. For example a case one day may show double vision, headache, and malaise, while two days later there may be no double vision but a distinct facial paralysis has appeared. Again a case may present irritability, myoclonic movements and sleeplessness to be followed in a few days by muttering or occupation delirium and still later may be lethargic and comatose. There may also be athetoid movements of the fingers and hand while the patient is in a deep lethargic state.

Without any special therapeutic treatment one finds that cases showing irritability and sleeplessness and athetoid movements tend to have a better prognosis than lethargic cases. Yet when lethargy has prevailed for about three weeks without any signs of failure on the part of the patient there is a distinct prospect of recovery. These however are only very rough indications in prognosis.

PROGRESS OF THE DISEASE.

As already mentioned a case may recover completely, it may temporarily recover only to relapse later, or it may pass directly from the acute to the chronic stage.

Whether the chronic stage is the result of relapse/

relapse or a direct prolongation of the acute it tends to appear in one of two forms:-

- (a) Parkinsonian Syndrome.
- (b) Striatal or Irritative Syndrome.

The former condition when well established is accurately portrayed in the classical description of the "Parkinsonian Mask". The second division forms a more or less new class of case not previously described or associated with any particular disease.

There is, however, no sudden arrival at those confirmed states, but a gradual progression from the simplest and almost negligible sign to an aggravated collection of symptoms. In the Parkinsonian Division the early signs may be slight mental dulness, lack of energy, pains in limbs, slowing of movements and speech, slight tremors and incoordinated movements.

The following case was admitted to Rawdon Convalescent Hospital in Sept. 1926 with a diagnosis of "Rheumatism".

Sam. W. aet 26.

On entering the surgery he advanced with a slow measured tread, his head slightly advanced and held firm. His face lacked expression and he stopped with a step half completed a few paces from me and then withdrew his advanced foot very slowly to the other. He did not offer any salutation. He gave one/

one the appearance of having been badly beaten and was sulking as a result. On interrogation his reactive time was slow and his enunciation was very indistinct and protracted. He complained of having pains all over his body and of feeling weak.

On further questioning he mentioned that he had had "Influenza" a year previously and had only worked for three months after his short incapacity when he was in bed for four days. He gave up work on account of weakness. At the time of admission he had suffered from those "Rheumatic" pains only for two months. There was no tremor or suggestion of headache.

Such a case would seem to be an intermediate in the path of the fully developed Parkinsonian Mask.

More pronounced were the symptoms in the case of Mrs M., admitted to Deanhead Sanatorium in Dec. 1926. She had suffered for numerous years from Bronchitis but although there was dulness of the right apex and an impaired note at the left Base there were no Tubercle Bacilli in the sputum. The patient had been bed-ridden for three months as a result of weakness and an intense headache which she said felt as if it would burst her head open. Her speech was very slow, slurring and indistinct; it lacked expression and did not vary in tone. She always had the one complaint:- "Oh! my head!"

There/

There was a constant twitching of the fingers but the arms were rigid and flexed in front of the body.

After a time she was encouraged to be up and moving about, when she showed the characteristic slow gait with fixed and bent head, staring gaze and expressionless face. If her limbs were raised she held them in that position for a considerable time and then they were unconsciously gradually lowered. When asked to walk backwards she commenced slowly and then her steps soon hastened until she struck and collapsed upon her bed.

The Parkinsonian Syndrome may be accompanied by atrophy of various muscle groups as is illustrated by the case of C.C. who had an acute attack in 1920 with apparent recovery. There was a relapse in 1924 and when seen in 1925 the patient in addition to the general signs could only trail his right leg up to his left because of atrophy of the Quadriceps Muscle on the affected side.

Epileptic Fits may also be an accompaniment as in the case of K. Kerr.

In 1918 she had a slight fever which was followed by an internal squint in the left eye and a fortnight after recovery a fit occurred. When seen in 1925 her face was dull and expressionless, skin glazed but/

but showed no wrinkles; skin was slightly lemon in tint. There was often a peculiar flushing above the eyebrows. The head was bent forward on the chest and the body arched anteriorly. The gait was characteristic. General intelligence was poor and reactive time slow, but the memory remained fairly good. The tone of her speech was plaintive and there was no accentuation of syllables.

Dizziness and numbness of the hands were the usual precursors of a fit and during the fit there was a marked Babinski sign on the right side.

On examination the right pupil was irregular in outline and sluggish in reaction but the left reacted normally.

Vertical Nystagmus was present in both eyes. Muscular movements were weak but there was slight rigidity of arm muscles on both sides.

STRIATAL OR IRRITATIVE SYNDROME.

This division roughly shows symptoms tending to the opposite pole from the previous group. Formerly we had depression, dulness and general inertia, now we face irritability and movements. As previously the symptoms may appear as a prolongation of the acute stage or occur as a relapse at a later date.

This irritability in mild form may only exist as/

as a slight mental change. The child who was formerly quiet at school is now restless and inattentive. In the adult we may have similar changes which however may give rise to serious difficulties in the home if they are not understood.

A few of these minor changes are evidenced by the case of Robertson who had an acute attack in 1918. with double vision, headache and delirium followed by unconsciousness for 14 days. Gradual recovery took place over a period of five weeks at the end of which the patient was able to resume his work. He now slept very soundly at night and required much more sleep to feel rested, including all Sunday. On returning from work until retiring to bed he proved to be very fussy and constantly worried about small household matters, which earlier would not have attracted his attention. Previously he could play with and amuse his children but now he was awkward in their midst and was inclined to be very impatient with them. At meal times he seldom enjoyed his food and often rose to examine some purchase or some article which attracted his attention, and then returned to his meal when his curiosity had been satisfied. Unfortunately these are only a few of the numerous changes which may occur and which so often become accentuated or magnified.

The/

The case of Mrs O'L. who had an acute attack in 1922 with apparent recovery after three weeks illness portrays additional symptoms which may arise.

After having resumed work for three months in normal health she began to feel tired and weak on return from work. This became progressively worse and was accompanied by a nervous twitching of the forefinger and thumb of the right hand.

When seen in 1925 there were myoclonic contractions of the fore finger and thumb of both hands and also of the forearms. The right shoulder was occasionally shrugged and the head moved to and fro. Attempt at movement controlled these contractions sufficiently to allow of the act being performed.

There was no fine tremor of the fingers.

A still further advance of this type of case is noticeable in the description of Lizzie L.'s condition in 1925.

In 1920 she had an acute attack with Double Vision, headache, and lethargy, but her recovery was apparently good.

In 1922 she developed severe headache with pains in the back and tremors of the hands which passed off periodically.

When seen in 1925 her expression was dull and heavy, her face puffy, and her forehead was frequently flushed. /

flushed. She spoke in a monotonous tone but could follow conversation very well.

The whole musculature of the limbs was in constant vibration from rhythmical contraction and relaxation. Her head was bent forward on the chest, her arms flexed in front of the body, the thighs bent towards the trunk and the leg flexed. Such was the position of rest which occurred for the fragment of a minute, only to be followed first by the finest of vibrations of the limb muscles. These vibrations increased in magnitude until the whole body shook with coarse myoclonic movements and then gradually faded until the position of rest was again reached for a few seconds. The intensity of the movements causes the bed to rock and rattle.

Those few cases have been mentioned only to indicate in a very small degree what may ultimately be the fearful and crippling results of the sequelae of Epidemic Encephalitis when no successful treatment is available.

PROGRESS OF THE DISEASE.

I have mentioned a few cases which have given a history of an acute attack with apparent recovery, and one has noticed that after a varying period/

period symptoms have again occurred. Then one is inclined to ask "Is the disease progressive?"

"Or if it is not progressive, does it produce some degenerative change within the brain which in itself becomes progressive?"

One is inclined to think that the disease, when a so-called relapse is noticed, is really steadily progressive, but the changes are so minute and gradual as to pass unnoticed until some other influence accelerates the process or calls the attention of the onlooker to a deviation from the normal in the person.

TREATMENT OF THE DISEASE.

Surely then, if the disease is progressive and can produce such devastating and agonising results, something can be done to arrest its cruelty.

On following the literature on the subject one finds that many methods have been adopted and numerous substances used in an endeavour to bring the acute disease to a rapid and successful issue.

Most essential in the treatment are absolute rest for the patient, absolute quiet, trained nursing and skilful feeding. So often in the acute stage the patient is in a semi-comatose or comatose condition when feeding becomes extremely difficult.

It/

It may have to be given by the feeding cup, by the spoon, or through a tube into the stomach, or it may even have to be given per rectum.

When given by the mouth one has found that beef-tea is the most generally useful, although sugar or glucose are extremely useful as they can be absorbed when administered per rectum.

If the cleanliness of the mouth is attended to and the nourishment given skilfully Broncho-pneumonia, which is so often the fatal complication, may often be avoided.

Care of the skin is essential especially in cases where there is incontinence of urine, to prevent bed sores and septic complications.

In addition to this essential care in the nursing of the patient many drugs can be administered to aid the process of recovery.

The production of shock by means of fixation abscesses or by serum has produced considerable temporary alleviation of symptoms, but it is questionable whether any permanent good is achieved by this method.

Antiseptics administered intravenously or magnesium sulphate intramuscularly or per rectum are amongst substances which have a distinct beneficial effect as also has horse serum.

Potassium/

Potassium Permanganate, given per rectum, in the hands of some observers has produced good results.

The general course of the disease is so uncertain that any drug or substance used may be credited with cure which, without its administration might have taken place. Naturally one is apt to incline to the beneficial effects of one's own Therapy and even to magnify them.

I have used Collosol Manganese in the acute cases, which I shall describe, sometimes aided by Magnesium Sulphate administered per rectum.

The former substance I have given as an antagonist to the infective agent, while the latter has been used for the temporary relief of intracranial pressure symptoms.

METHOD OF ADMINISTRATION OF COLLOSOL MANGANESE.

When the drug is injected subcutaneously it produces an immediate sharp pain which is followed by swelling and redness in most people. The swelling lasts from one to three days and gives rise to pain and limitation of movement.

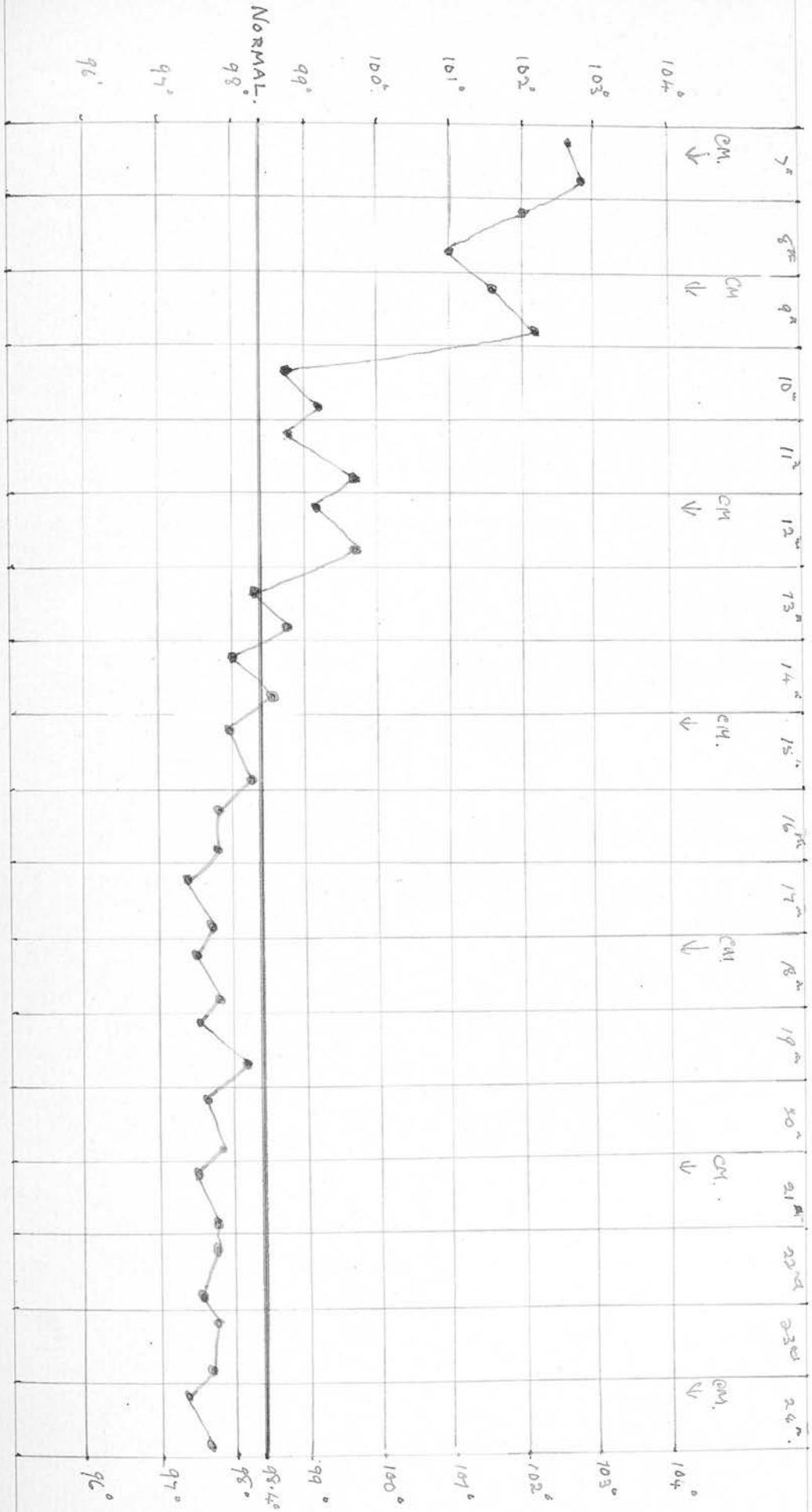
Given deeply intramuscularly, however, there is no/

no pain, no stiffness and no limitation of movement.

I have used this intramuscular method holding the skin tight and stretched with the left thumb and piercing the needle sharply into the muscle to a depth of $\frac{3}{4}$ to 1 inch. If a sharp needle is used and the insertion of the instrument is rapid no pain is felt.

I have made use of Crooke's Collosol Manganese and have limited the dose to one c.c. at an interval of from three to four days.

The drug administered in this way produces a more or less continuous effect even to the extent of being slightly accumulative. It may be found necessary to push the drug to the extreme point of tolerance which is indicated by difficulty of swallowing, dryness of the mouth and throat, sore tongue and constipation. When these symptoms appear it is advisable to give a complete rest from injections for seven days to allow of the accumulated Manganese being eliminated from the body.



THE ADMINISTRATION OF COLLOSOL MANGANESE IN
THE ACUTE FORM.

In the following few cases I shall endeavour to describe the main symptoms, the time of administration of the drug, and the effects produced.

CASE I. Madge W. Aged 13.

Admitted to Hospital 17th June 1924.

Onset. 7th June. Sleeplessness, double vision and severe headache.

On Admission:- General appearance;- restless moving of the head from one side to the other, eyes closed, twitching of the hands and arms, continually moving about the bed clothes.

When spoken to loudly she responded and took notice for a moment but said nothing. When asked to hold a piece of paper in her hand she did so, and it was then noticed that the clonic movements of the fingers and hands were greatly exaggerated. The paper could be held quite firmly. The thumbs were flexed at all joints and crossed the palms. The arms were easily flexed but when one attempted to extend them afterwards there was a distinct resistance from the flexors at the elbow, and when force was applied clonic/

clonic movements were elicited. Flexion at the wrists also produced clonus.

Both legs were rigid, the extensors and flexors being in spasm which was overcome by two or three passive movements only to return on rest. The Knee Jerks on both sides were markedly exaggerated while Babinski signs were present. Other Reflexes were all active.

Eyes:- Pupils equal and regular - reacting normally.

No nystagmus or strabismus. No ptosis.

There was no paralysis.

Saliva was markedly increased in flow.

Tonsils:- congested.

Pulse:- rapid and weak. 135 P.M.

Temperature. 102.8.

Patient commenced to mutter to herself but no words were audible.

1 cc. Collosol Manganese administered on admission. She was delirious at night, tried to get out of bed and did not sleep.

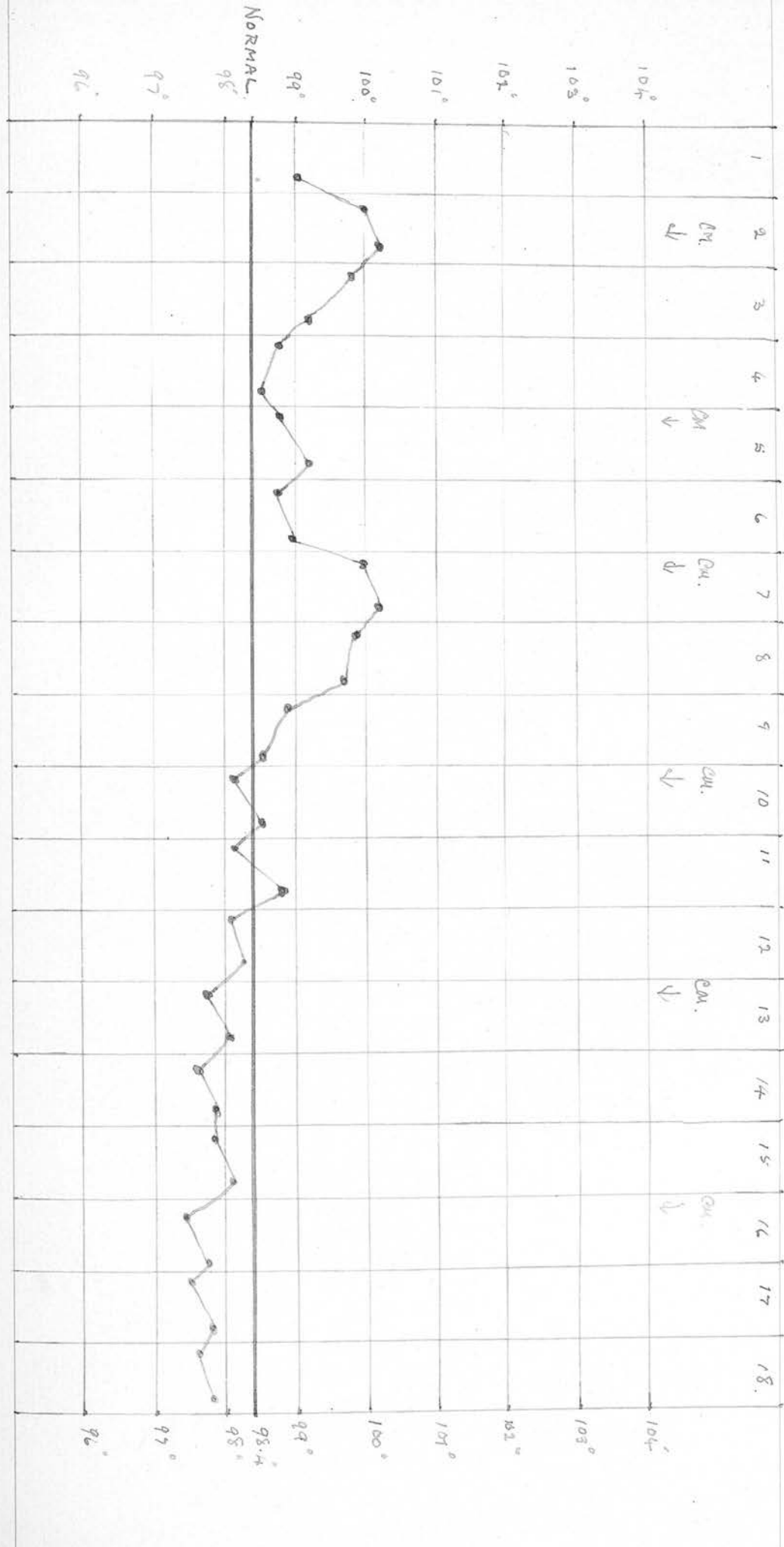
The following morning she was slightly brighter, was able to speak, and complained of severe headache. Magnesium Sulphate in saturated solution was given as an enema without any relief.

Lumbar puncture was performed and the cerebro-spinal fluid issued under pressure but was absolutely clear./

clear. 10 ccs. were run off and the patient was much relieved and slept.

After the second night in hospital the temperature had dropped 99. and the patient seemed very quiet, took food when it was offered and showed a greater tendency to sleep. An erythematous punctate pink rash developed over the lower abdomen and buttocks but disappeared on the 3rd day, to be followed by a very faint desquamation.

1 cc. Collosol Manganese given on the 3rd day was followed by a slight rise of temperature and then a subsequent greater fall, below 99. Drowsiness of the patient became apparent and the spasm of muscles was increased in intensity. There was increased flow of saliva. On the sixth day a further injection was given and 36 hours later there was a marked improvement in the general condition of the patient. She spoke better and swallowed easier, and was generally more normal. However her appearance was expressionless and reactive time slow. Spasm of muscles had absolutely disappeared and there was no tremor. The patient progressed slowly each day and her temperature remained subnormal. There was no headache and her appetite improved, but there was still a slight tendency to the Parkinsonian Mask. After two further injections at the same interval the patient was allowed up when her gait was very slow/



slow; but as she gained strength there was not any difference in her walking which seemed to be laboured. With continued treatment this difficulty decreased and when her ninth injection had had effect there was no evidence of the Parkinsonian Syndrome.

She was discharged from hospital and evidence one year later showed that she seemed perfectly normal.

CASE II. Miss S. Aet. 28.

History:- Patient felt occasional pains in epigastrium during the afternoon but at 11 p.m. the pain became extremely acute and when seen at 11.30 p.m. she was lying in bed in a semi-comatose condition and slightly cyanosed. Her head moved restlessly from one side to the other and there was marked excretion of saliva. Every now and then her lower jaw muscles went into clonic spasm, each contraction of the Masseter muscles increasing in intensity until the mouth was firmly clenched and could not be opened manually. The tongue had been severely bitten during one of these spasms. There was considerable neck rigidity and hiccough was seen to coincide often with the spasm of the Masseters.

Food_Poisoning was suspected and the stomach was thoroughly washed out; and before withdrawing the tube 1 oz. of castor oil was run into the stomach.

$\frac{1}{4}$ grain of morphia was given as a sedative.

Hiccough and vomiting ceased for three hours and when the patient was seen the following morning she was in a delirious state, fumbling with the bedclothes, trying to get out of bed, helping to clean the room, and going through the process of washing dishes while in bed.

The right hand twitched and the arm was flexed at the elbow. Attempt at extension elicited marked resistance of the flexor muscles, particularly the Biceps, and clonic contractions commenced.

Clonic contractions of the jaw were not so marked as on the previous evening, but at once became violent when the jaw was forced down.

Hiccough and sickness had ceased to annoy the patient at mid-day but double ptosis had become established with medial strabismus of the right eye and left facial paralysis. She was able to speak and could protrude her tongue which was tremulous and thickly furred.

Lumbar puncture was performed and a clear fluid issued under normal pressure. Knee and ankle jerks were both exaggerated. Ankle clonus was present but the plantar reflexes were normal.

There was incontinence of urine and faeces.

The diagnosis of Encephalitis Lethargica was made and 1 cc. of Colloidal Manganese injected intramuscularly.

The/

The Temperature had risen from 99 when first seen to 100 at the time of injection.

The following evening the temperature had fallen to 99 and the delirium had lessened. Clonic spasms were not evident and the patient's mental condition has improved sufficiently to allow of her describing her own feelings. She complained particularly of frontal headache and pain in the neck and shoulders.

4th Morning:- Temperature 98.6.

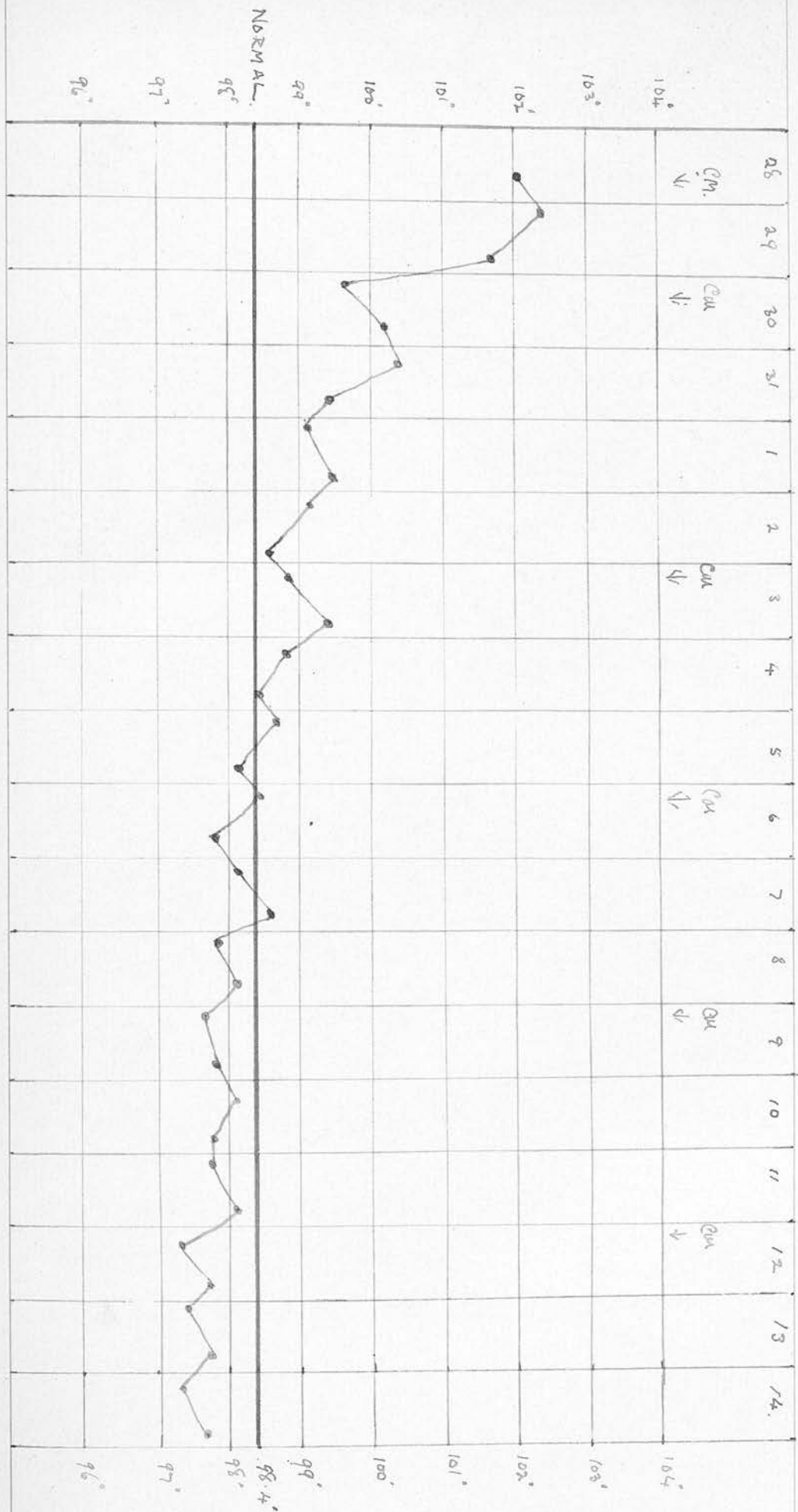
Her general mental condition was greatly improved and she recognised her own parents and realised she was in bed, but could not understand the reason why she was not allowed to rise. She was always on good terms with her parents but she ordered them out of the room for no apparent reason. She ordered ham and eggs for her tea.

The twitching of her hands and fingers was still present, as also was the muscular resistance to passive movements of the limbs. There was no incontinence and she asked for the bed conveniences when she required them.

She was able to drink diluted mild and retained it.

On the 5th day a second injection was given and that night she was exceedingly comfortable although her temperature had risen to 99. She was able to take chicken broth and enjoyed it. The headache and ptosis/

26. A.



ptosis had gone and there was distinct improvement of the facial paralysis. She spoke without slurring but slower than normal. There was still resistance to flexion at the extremities.

There was progress until the 7th morning when the temperature began to rise and an injection of Manganese was given at night when the temperature had reached 100.2. Then the patient was dull, asked for nothing and would take no nourishment. During the night there was again incontinence which persisted throughout the 8th day. On the 9th day however the temperature had again begun to drop and the patient was much better. She took sips of milk and beef tea and offered a few remarks. At night the temperature had returned to normal but still resistance of the leg muscles persisted with exaggerated knee jerks. Four more injections were given at three day intervals and recovery was gradual without any apparent ill-effects.

CASE III. Jessie R. Aet. 12.

Onset on May 24th with "dim" eyesight, twitching of face and arms, headache and pain in back and weakness.

Admitted to Hospital on 28th May 1924.

General appearance:- Face, body, arms and legs showed fine fibrillary twitching, and in addition/

addition coarser jerking movements of the hands and arms were noticeable. Patient appeared listless, could not think clearly and did not recognise her surroundings. Her memory of recent events was distinctly impaired and she could not say whether she had any brothers or sisters.

Temperature 102. Pulse 100.

Collosol Manganese given intramuscularly.

On the following day (29th) Pupils were both dilated but reacted to light, no deviation from the normal line of vision, and no nystagmus. There was no ptosis. The fibrillary twitchings had almost vanished but the clonic movements of the thumb and hand were still evident. There was distinct spasm of the flexor muscles of the arms and pulling against this resistance elicited clonic movements. The resistance however was overcome by a few passive movements.

Knee jerks ++

Ankle Clonus present.

Plantar Reflexes:- Extensor on both sides.

Distinct spasm of flexors of the leg easily overcome by movements but no clonic contractions resulted.

Collosol Manganese again given.

30th Patient was quiet and drowsy but could be easily awakened. The headache had gone and there were no twitchings or clonic movements. The body reflexes/

reflexes were more normal. There still remained a slight flexor spasm of the arms.

Pupils were more normal in size and the patient could read large print; and letters below a quarter of an inch in length were indistinct.

During the following three days the patient remained drowsy but gradually indicated a liking for beef tea and other nutritious foods. She offered a few remarks about her bed clothes and asked for her mother.

3rd June. Collosol Manganese administered and on the following day there was a distinct brightening of the patient's disposition. She moved about in bed attempting to make herself comfortable and her bowels which tended to be constipated became more regular. All traces of spasm of muscle had passed off and the eyesight gradually improved.

Injections of Manganese were given on the 7th and 11th of June, by which time the patient was able to sit up in bed, and could read a book of ordinary print. She was eating well and was inclined to be active in bed. Her memory for recent events had become quite clear and she could talk clearly although slowly. Her facial expression was serious.

The treatment was continued and on the 17th June/

June her facial expression was normal and she smiled on approach. She walked straight with her eyes closed and could walk backwards without tending to hasten. Her appetite was now seldom satisfied and she appeared absolutely well.

CASE IV. Mrs John K. Aet. 28.

Onset: 10th June 1924 with dizziness, double vision, severe headache, pains in joints and back, delirious at times.

Admitted 16th June. Patient found to be two months pregnant but there was no albuminuria, no swelling of the ankles, and no cellular element in the urine. No dyspnoea.

She was drowsy and very difficult to wake, but when she did hear she made a suitable response and then fell fast asleep. She now only complained of a severe headache and said her other symptoms had gone. She would only be persuaded to drink a teaspoonful of water occasionally.

On examination there was no paralysis, but there was evident spasm of the flexors of the arms which could not be overcome, and the thumbs were often sharply drawn across the palms. The reflexes of the/

the body were slightly exaggerated and there was evidence of incontinence of urine.

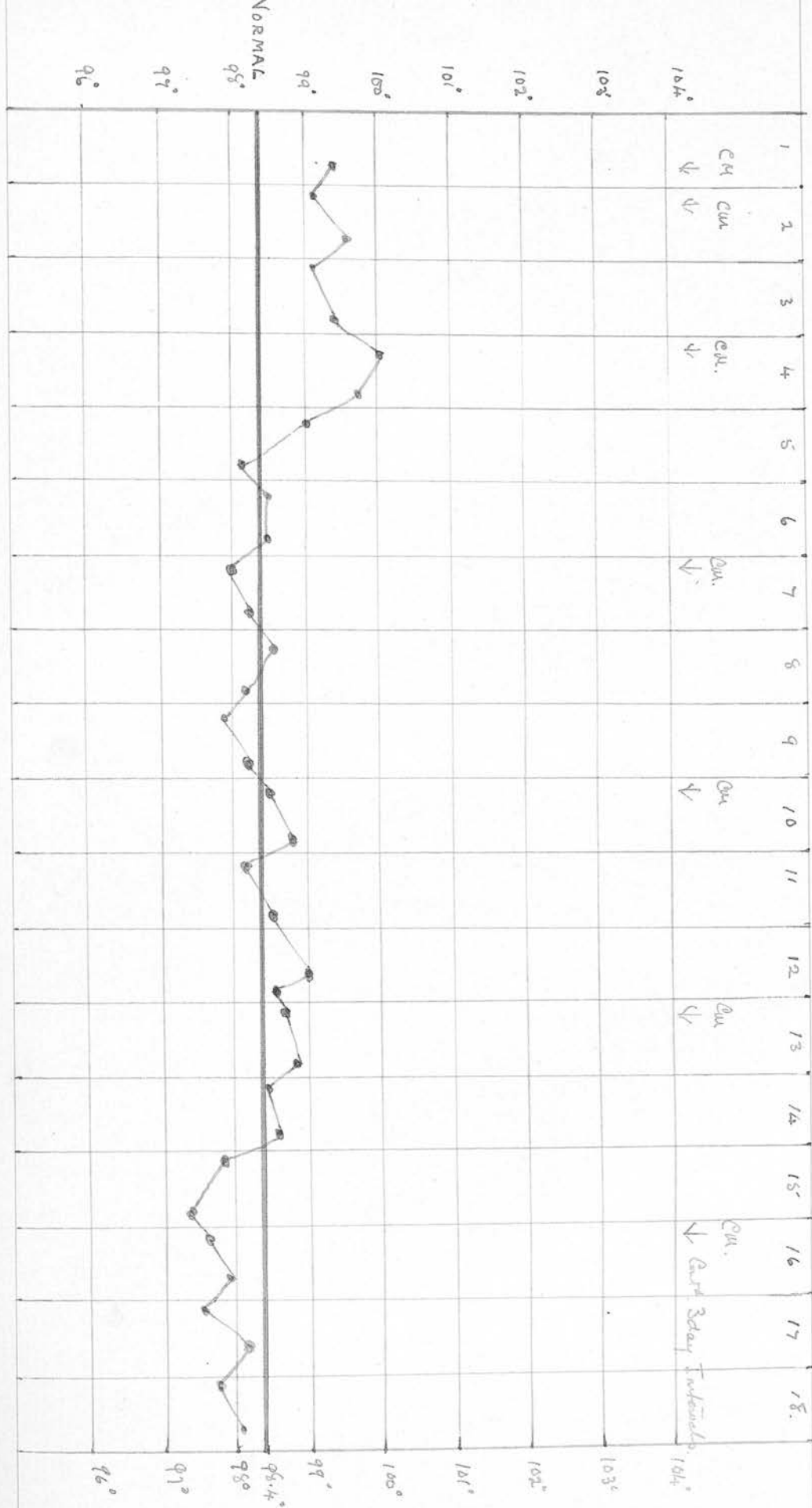
Collosol Manganese was administered intramuscularly, while saturated magnesium sulphate was infiltrated per rectum as a warm solution.

On the following day the patient appeared much brighter but now realised her two children had been left at home and worried unduly as to their safety. She could drink quite well and enjoyed a small quantity of beef-tea. She could see to read large print for a few moments and then her sight dulled. Her arms were still stiff but there was no twitching of the thumbs.

On the 19th she was again given an injection, and on the 20th all signs of lethargy had gone. There was no muscular rigidity but her eyesight was still poor.

After her treatment on the 22nd the patient was able to be up, and only complained of the weakness of her limbs. There was no difficulty of vision or signs of headache, and her mental condition seemed quite normal.

Two additional injections were given and she was discharged on the 30th of June when there were absolutely no signs of the disease.



CASE V. Janet M. Aet. 8.

Admitted to hospital after eight weeks duration of the malady, the onset of which was treated as influenza. The patient however was irritable, restless, did not sleep, and feeding was difficult, with the result that wasting occurred rapidly.

(Strangely enough she was admitted to hospital at the same time as another case with a long history of suffering and thought to be a case of Epidemic Encephalitis. This latter case had no irritability with the exception of a constant rolling movement of the head. There was medial strabismus of a week's standing but the pupils reacted. Headache seemed to occur in agonising spasms causing the patient to struggle and bury her head in the pillow, and grasp the bedclothes with her outstretched arms. Her abdomen was protuberant and her lungs showed numerous moist sounds at the bases.

A diagnosis of Tubercular Meningitis was made in this case, but it illustrates the similarity of Tubercular Meningitis to a Chronic Encephalitis especially when both conditions are seen at a wasted stage.)

On admission: She was drowsy and difficult to waken. She only complained of severe headache. Her face was pinched and expressionless and her thumbs twitched, especially when she was disturbed.

The neck muscles were rigid and painful.

The flexors of the legs and arms were in spasm.

The body reflexes were exceedingly active.

Lumbar Puncture was performed to relieve the intracranial pressure and for diagnostic purposes, and a clear fluid issued under considerable pressure. This was examined and found to contain very few cells and no organisms.

Collosol Manganese was given on the night following her admission, and on the following day her temperature had dropped to normal but without any apparent improvement in her condition. There was incontinence of urine and also of faeces. She however took sips of beef-tea and occasionally a little jelly. A further injection was given on the second day, and within thirty-six hours there was a distinct improvement in the general attitude of the patient. She was able to drink more easily and her movements were not so clumsy. Her headache was considerably relieved.

Injectons were given at three day intervals
for/

for twelve days, during which period little improvement was noticed, her feeding was difficult and the incontinence continued.

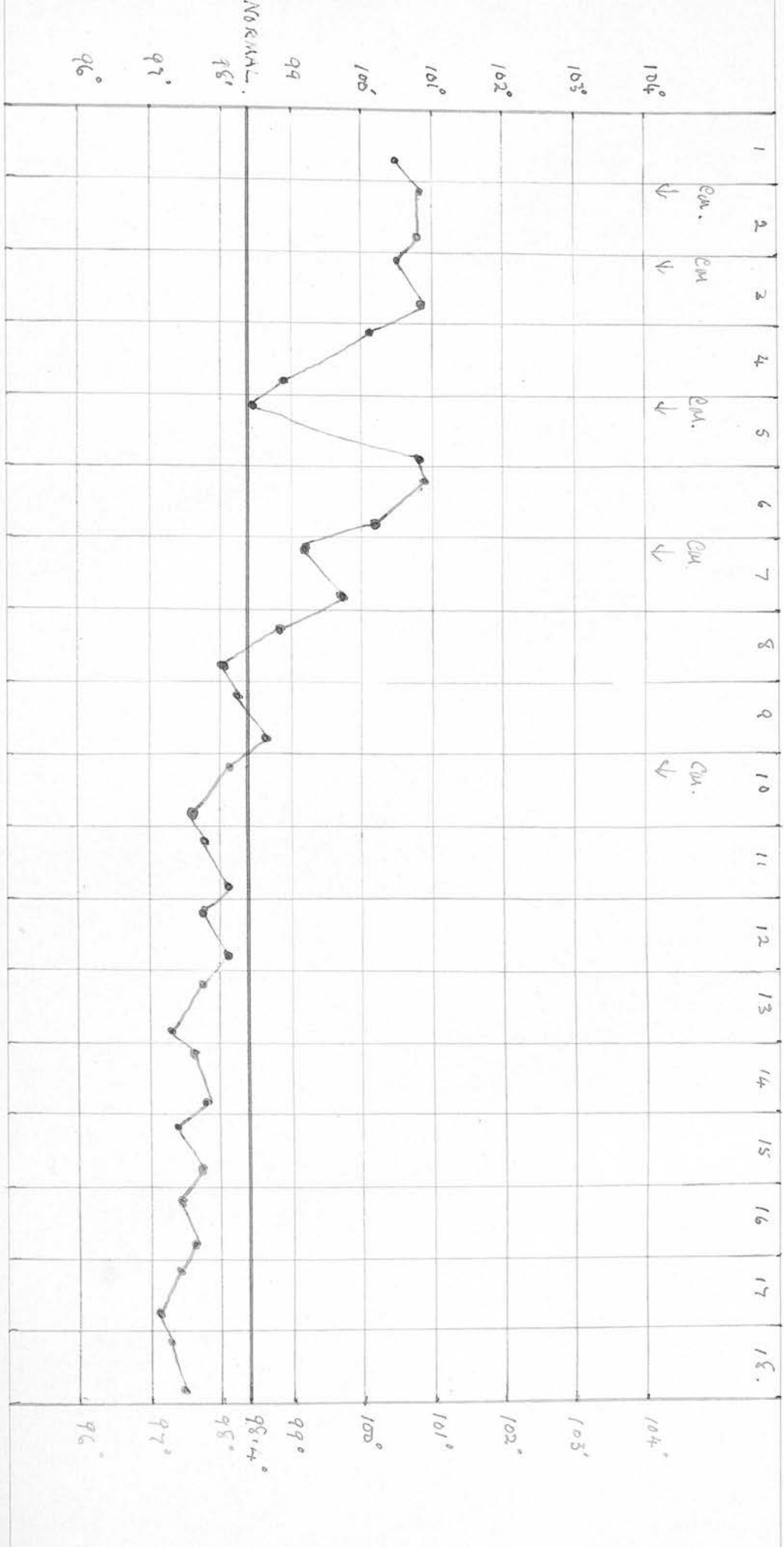
Then, however, the rigidity of her neck muscles was considerably released and the persistent headache disappeared.

Within the following two days she improved sufficiently to be able to talk coherently and to take more food. The incontinence ceased but the spasm of the arms and legs was still pronounced and gave rise to pain.

Manganese was continued and at the end of five weeks in hospital she was able to be out of bed and could enjoy her food. There was still considerable difficulty in controlling the movements of the arms and legs, but there was no rigidity. After seven weeks she was able to walk out of hospital quite briskly.

CASE VI. Mrs B. Aet. 65.

Onset:- Intense neuritis ascending on either side of the neck and reaching up behind the ears. This continued for ten days and was followed by weakness and loss of appetite. She felt miserable and retired to bed, and for ten more days she seemed to get gradually worse and eventually/



eventually passed into a semi-comatose state with nocturnal restlessness. She attempted to jump out of bed as a result of sudden impulses to handle or do something. There were also muttering delirium, picking at the bed clothes, involuntary twitching of the thumbs and arms.

At this stage she was seen by Prof. Bramwell who made the diagnosis of Encephalitis Lethargica.

The patient's condition gradually passed from the irritative stage with stiffness of muscles and myoclonic movements to one of semi-coma with incontinence of urine and faeces. She still responded when spoken to loudly, and answered correctly, but did not remember objects or facts. Then coma set in and the patient neither spoke nor answered when spoken to.

Liquid food had to be run into her stomach in small quantities. She had been in this condition for 14 days when Manganese therapy was commenced.

After the third injection at two-day intervals there was an encouraging improvement in the patient's swallowing. The twitching movements of the thumb and forefinger were seldom seen. The treatment was continued every third day and the improvement and clearing of the brain was extremely rapid, so that at the end of twenty days injections the incontinence had/

had ceased and the patient was eating well.

There was, however, a slight return of the incontinence of faeces and this persisted for a time after the patient was able to be up. Manganese was continued until there was dryness of the mouth and difficulty of swallowing, - twenty-eight days after its commencement.

At the end of this period - two months from the onset of symptoms - the patient was still very emaciated, showed a lemon tint of the skin but no muscular or mental defects as a result of the infection.

She is now absolutely well and has had no relapse within the four years since her attack.

CASE VII. Mrs H. Aet. 52.

Onset:- Patient developed a gradual faint feeling while sitting in a chair by the fire side. She retired to bed and on lying down became violently sick and vomited.

When seen at night there were spasmodic contractions of the diaphragm with expulsive vomiting with each contraction. Between these attacks she remained in a senseless condition, but her arms were very restless and her fingers clutched and folded the bedclothes.

Temperature 100.5

Pulse/

Pulse 60.

Respirations 19.

Patient was given 3 grs Calomel.

On the following morning she was comatose, did not recognise anyone but could answer when spoken to. The speech was delayed and slurred and the patient had the greatest difficulty in finding the words she required.

There was ptosis on both sides and the neck muscles were rigid, retracting the head. The arm muscles were in spasm and clonic movements were seen when pressure was exerted against the spasm. She constantly tried to fold the bedclothes but did not look to see what she was doing.

Pupils were dilated but regular in outline and equal in size. There was no strabismus.

Knee Jerks were markedly exaggerated and the plantar reflexes were extensor. There was incontinence of urine and faeces.

Temperature 100.8.

Manganese was administered in the usual method and again the following day. The patient remained in much the same condition but the ptosis had gone. There was muttering delirium and restlessness, patient attempting to get out of bed to cook a meal. She perspired freely and she insisted on discarding all/
all/

all bed coverings. The body reflexes were now very active.

A further injection was given and on the following day a distinct improvement of the patient's condition was noticed. She was very much quieter, agreeable to swallow liquid food and spoke in reply to my interrogation as to her feelings. She said she had a very severe headache and her neck was painful. The temperature, although it had dropped to normal after the first two injections, was now running about 101, but the pulse was slow as were the respirations.

A fourth injection was given on the 6th day and afterwards the temperature gradually fell to below normal. Coincident with this there was a gradual improvement in the mental condition of the patient. She began to notice when one moved in the room and was soon able to recognise her husband. This recognition was only momentary to begin with, for she immediately shut her eyes and turned her head away as if to fall asleep and made no further comment; but gradually her brain became more active and clearer and she was able to interest herself in outside affairs for five minutes or longer.

The bowels however were very stubborn and when an aperient was given incontinence of faeces persisted until a week after the patient was strong enough to be up, although the bladder had regained its normal control. /

control.

Further injections were given and at the end of sixteen days the patient was allowed out of bed for the first time, when she complained of extreme weakness of her legs and back. There was, however, no muscular spasm nor tremor, and the headache was absolutely relieved.

Progress was slow but when heard of two years later the patient was able to attend to her farm duties as before without the slightest trace of any sequelae of the disease.

CASE VIII. Mrs W. Aet. 28.

Onset:- Patient had a difficult forceps delivery of a live child in a nursing home.

History:- As far as could be gathered from relatives the patient after delivery was relatively well except for profound weakness which was not accountable for by haemorrhage. On the 10th day she had a "shiver" with about five minutes unconsciousness and when her brain cleared she found she had lost the power of the right arm. Subsequently she had severe headache and was exceedingly restless. This restlessness continued over night with the result that she could not sleep.

There was evidently no noticeable rise in temperature/

temperature as the patient was allowed up on the 16th day and her condition regarded as neurotic.

The power gradually returned to the right arm and twenty-four days after confinement there was a second "shiver" with loss of power of the left side of the body.

She was confined to bed and as on the right side the power was gradually restored to the left.

Four weeks after her confinement she had another similar "shiver" but this time she did not seem to regain consciousness as previously.

I was asked to see her and she was seen to be in a drowsy state but answered when spoken to and she could recognise all in the room.

Temperature 100.5.

Pulse 60.

Respirations 19.

Pupils were both dilated but reacted to light, but slowly to accommodation.

There was no paresis of the facial muscles and the tongue could be protruded easily and straight; it was, however, thickly coated.

The neck muscles were rigid and tender to pressure and retracted the head slightly.

The left arm was rigid and clonic movements were produced by attempt to extend the elbow.

There were no chest symptoms or signs.

The/

The left leg was slightly rigid in extension but easily flexed.'

The Knee Jerk on the left side was extremely exaggerated and the plantar reflex was extensor.

There was incontinence of urine and the bowels had not moved. An enema was given with good result, but half an hour later there was slight incontinence of faeces.

1 cc. Collosol Manganese was injected intramuscularly and a similar dose was repeated on the following morning.

She had had her first restful night since confinement but one realised that she had now passed into the lethargic state and was very difficult to feed. The next day she was much brighter after a comfortable night and she was able to drink beef tea of her own accord. The stiffness of her neck had relaxed and she was able to bend her head forwards although there was considerable tenderness in doing so. Her temperature was now normal and she seemed to have better control over her bladder. The left knee jerk was not so active, and any plantar reflex was difficult to elicit. The patient was able to flex her left leg for the first time since losing its use.

Manganese was again injected and for two days there was a very pleasing improvement but suddenly the temperature rose to 100 and an irritating cough was/

was noticed.

Counter-irritants were applied to both sides of the chest but in the morning consolidation was suspected at the root of the left lung when the temperature had reached 103.2° , pulse rate 100, and respirations 35 p.m.

In the evening there were definite signs of consolidation at the left base and the patient expired as a result of the Broncho-pneumonia.

C O N C L U S I O N .

In the treatment of Acute Encephalitis with Collosol Manganese intramuscularly one notices a most remarkable mental change within 24 to 36 hours after the administration of the drug.

If the case is irritable there is a distinct calming of impulses passing from the brain with the result that myoclonic movements and tremors become less evident and the general restlessness of the patient is soothed.

In the lethargic case the alteration is the reverse, when there is general brightening of the mental condition, a better response to stimuli, and a more rapid appreciation of them.

Those two undoubted facts indicate a definite inhibitory effect on the progress of the disease if not indeed an antagonistic one.

If the temperature is elevated there is usually a slight rise following the injection but a definite fall later coinciding with the mental improvement. When the temperature is normal or subnormal there may be a slight rise after the injection, but there is/

is no further fall as is the case when the temperature is elevated.

As far as I have been able to trace these cases described there have been no sequelae which indicates that the treatment adopted has a definite effect in stopping the progress of the disease.

Considering the last case described, one is inclined to think that if pneumonia had not intervened cure would have been established.

This treatment has been attempted in old-standing chronic cases of the disease without any beneficial effects, and one therefore comes to the decision that, if cure is to be expected, the treatment must be commenced at an early stage in the acute attack and continued although the first or second injection may not produce any distinct and evident relief.

